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Research Submission

Non-Pharmacological Treatment for Primary Headaches Prevention and Lifestyle Changes in a Low-Income Community of Brazil: A Randomized Clinical Trial

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Background.—Primary headaches can be reduced by lifestyle changes, such as stress management and physical activity. However, access to programs focused on behavioral interventions is limited in underserved, poor communities.

Objectives.—We performed a randomized open-label clinical trial to test the therapeutic and behavioral effects of aerobic exercise, relaxation, or the combination of both, in individuals with primary headaches of a small, low-income community of the Brazilian Amazon.

Methods.—Participants were screened from the riverine/rural population, and individuals with primary headache were included. We assessed clinical characteristics and physical activity levels. Interventions were delivery 3 times/week for 6 months. The primary outcome variable was changes in days with headache, while changes in duration of attacks, pain intensity, and physical activity levels were secondary outcomes variables.

Results.—Seven hundred and ninety individuals were screened (15.3% of rural/riverine population). Seventy-four participants were randomly assigned to relaxation (n = 25), physical activity orientation program (n = 25), or both (n = 24) interventions. Intention to treat analyses showed all interventions as effective to reduce days with headaches and duration of attacks (both $P < .01$). Pain intensity was reduced only in relaxation and relaxation + physical activity groups (both $P < .01$). Physical activity levels increased only in the relaxation + physical activity group ($P < .05$).

Conclusions.—Non-pharmacological interventions such as physical activity and relaxation are effective for reducing headaches, while combining such interventions promote health behavior toward higher physical activity levels in low-income populations with primary headaches.

Clinical Trial Registration number: SGPP 1544.

Key words: pain management, migraine, tension-type headache, physical activity, relaxation, health behavior

Abbreviations: ANOVA analysis of variance, IPAQ international physical activity questionnaire, MET metabolic equivalent of task, PA physical activity, RLX relaxation, RLX+PA relaxation plus physical activity

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INTRODUCTION

Primary headaches affect a substantial proportion of the general population worldwide,[1] representing a leading cause of years lived with disability.[2] In Brazil, migraine[3] and tension-type headache[4] affect

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15.2% and 13% of population, respectively. Regarding primary headaches in Brazil, we have previously reported in a nationwide study a higher odds ratio for having migraines in people with lower household income, which may reflect limited access to adequate treatment and lack of specific programs for patient education.[3] Even in the public health system of developed metropolitan areas in Brazil, nearly 30% of patients do not receive any headache preventive treatment.[5]

Multidisciplinary, non-pharmacological, interventions for primary headache prevention may be effective to optimize clinical response, and may help to overcome the lack of access to specific headache preventive pharmacological therapies.[6-8] Also, such approaches may promote health behavior such as increased physical activity, albeit studies have been limited to tertiary clinics settings.[6-8] Promoting health behavior and lifestyle changes, including management of perceived stress through relaxation,[6-11] and increase physical activity levels through aerobic exercise,[12-16] has been shown to be effective to improve clinical outcomes in primary headache disorders.

However, there is a gap in the literature concerning the effects of multidisciplinary non-pharmacological interventions through aerobic exercise and relaxation on headache clinical outcomes, and changes in physical activity levels in low-income communities. Interventions targeting these outcomes in low-income populations are needed, particularly in underserved areas, wherein primary headaches are highly prevalent.[17,18] For example, we reported an inverse correlation between physical activity and headache frequency,[3] whereas another population study in Brazil showed a positive correlation between household income, educational level, and physical activity level, with the lowest physical activity levels among people in the lower socioeconomic strata.[19] Moreover, another epidemiologic study with the Norwegian population found an association between low cardiorespiratory fitness and prevalence of primary headaches.[20] For perceived stress, it is well-known that socioeconomic status has a prominent role on stress-related diseases, and perceived stress constitutes the most consistent trigger factor for primary headaches.[21,22]

Therefore, in order to test the response of a lifestyle change program through aerobic exercise orientation/counseling and relaxation on clinical outcomes in people with primary headache, we designed, together with local public service workers, a community-based screening and non-pharmacological interventions in a low-income population area of the Brazilian Amazon. We hypothesized that both aerobic exercise and relaxation interventions would promote significant reductions in primary outcome variable, and the groups receiving aerobic exercise would change health behavior toward increased physical activity levels.

METHODS

Study Design.—This is a randomized, open-label, clinical trial to test the preventive effect of a 6-month non-pharmacological program through physical activity (PA), relaxation (RLX), or physical activity plus relaxation (RLX+PA) on primary headaches, and changes in physical activity behavior in a low-income population. The study is part of a broader project and social initiative to promote headache education to the health care professionals of the public health care system, and implementation of preventive programs through patient education and multidisciplinary non-pharmacological interventions (Figure 1). The study was conducted between April 2013 and December 2014 in the riverine community of Novo Airão, a small city located at the Brazilian Amazon, State of Amazonas, Brazil. The population in the riverine/rural area is 5224, and the city's Human Development Index is 0.57, with a gross domestic product per capita of US$ 1607/year.[23] In the riverine area, this economic index is significantly lower and the majority of families live with government social welfare.[23]

The rationale for choosing this area was to test the feasibility of implementing low-cost non-pharmacological inventions for headache prevention in places where limited health care is available, but having public health service workers and other public service professionals able to assist in the supervision of interventions. We mobilized a nurse, a social service officer, and an elementary/physical educator teacher to help our research group on data collection and supervision of interventions. Before implementing the interventions, the public service workers were

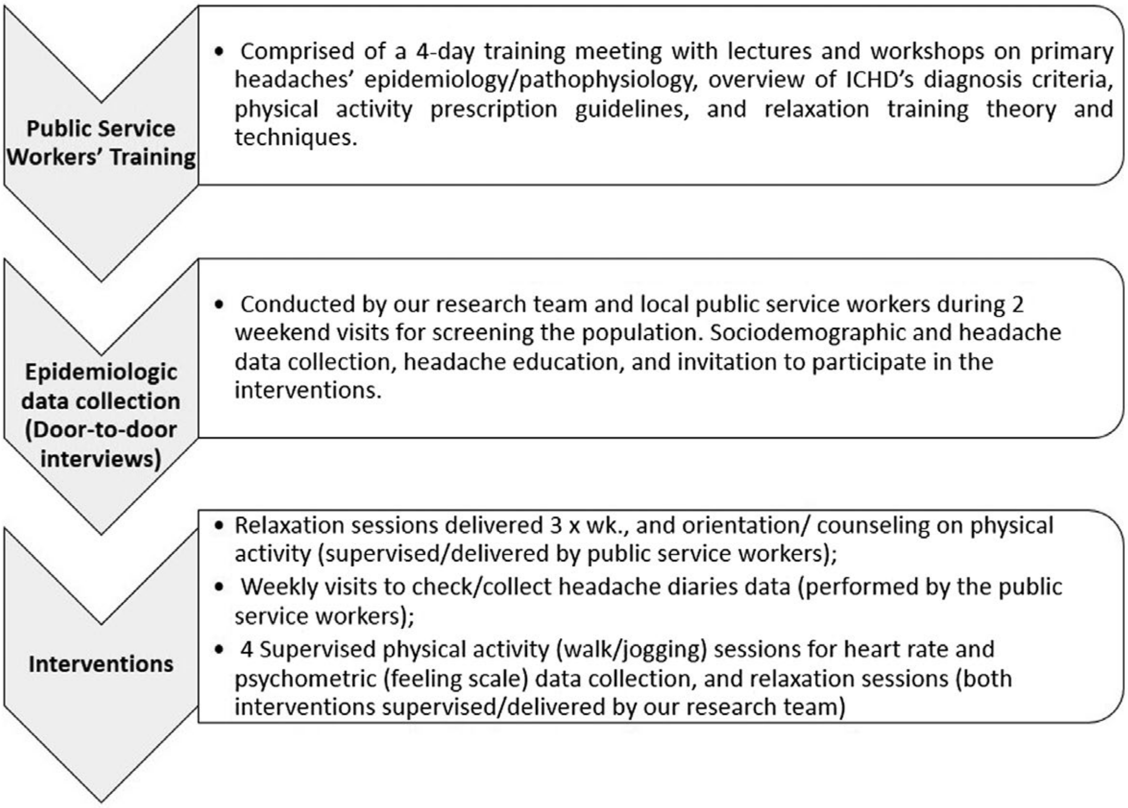

Fig. 1.—Stages of the social initiative project until the implementation of multidisciplinary non-pharmacological interventions.

trained by our research group through lectures and workshops addressing the ICHD's criteria for primary headaches, pathophysiology and epidemiology, headache diary data, outline of the current guidelines for exercise prescription, and relaxation theory and techniques.

Our group and the public service workers conducted door-to-door household surveys with clinical interviews to gather information on headache prevalence and diagnosis, and to promote patient education for headache prevention, including specific instructions on how to fill headache diaries. The population surveyed was invited to participate in the interventions.

The participants that agreed to engage in the interventions were assessed for clinical headache outcomes and physical activity levels at baseline and after 6 months. Due to the low educational levels of the participants, the public service workers contacted them on a weekly basis for checking the headache diaries (paper-based diary). Relaxation sessions were delivered 3 per/week (group sessions), and physical activity orientation/counseling was delivered on visits for checking headache status (PA group), or at relaxation sessions (RLX+PA group).

All participants signed informed consent, and the study protocol was approved by the Ethical Research Committee of the Albert Einstein Hospital. This study complies with the CONSORT's Statement for non-pharmacological trials.[24]

Participants.—The inclusion criteria were individuals that agreed to participate in the study, from both sexes, aged between 18 and 65 years, who were diagnosed with some form of primary headache (presenting with headache frequency >2 per month), according to ICHD-II.[25] We excluded patients with suspected secondary headaches.

Interventions.—Relaxation.—Relaxation sessions were delivered at classrooms of a public school by researcher JPPM. Relaxation training and learning relaxation techniques can be effective in reducing physiological hyperarousal in the patient.[26] Relaxation practice involves practicing relaxation techniques during the day, prior to bedtime, and in the middle of the night, if the patient is unable to fall back asleep. Common relaxation techniques include progressive muscle relaxation, which involves alternately tensing and relaxing different muscle groups in the body; deep breathing techniques, which involve diaphragmatic breathing; body scanning, which involves focusing on a body-part sequence that covers the whole body; and autogenic training, which involves visualizing a peaceful scene and repeating autogenic phrases to deepen the relaxation response.[26]

Physical Activity Orientation Program.—The participants allocated to the physical activity program were instructed to walk/jog for 20–30 minutes, 3 times a week, at a self-selected intensity. On 4 separate visits, we conducted supervised exercise sessions with heart rate monitoring (wearable heart rate monitor F5, Polar Electro®, Finland) and psychometric measurements (affective response), conducted at the schoolyard by researcher ABO in the beginning and in the middle of the intervention period (Figure 1). We chose self-selected exercise intensity because this intensity has shown increased affective response, that is, increased feeling of well-being and pleasure with exercise, which is associated with higher adherence to physical activity participation.[27-31] Participants were instructed to exercise at the intensity they would feel comfortable, but capable of perceiving changes in bodily signals such as ventilation and perspiration. We analyzed the exercise session's average heart rate, and the affective response before, at the 10th minute of exercise, and immediately after the exercise cessation.

A Feeling scale was used to assess the affective response.[32] This is a Likert-type scale of basic affect, ranging from 5 to −5, with descriptors at odds integers and zero (5 = "very good," 3 = "good," 1 = "fairly good," 0 = "neutral/indifferent," −1 = "fairly bad," −3 = "bad," and −5 = "very bad"). We chose this scale because it is composed of verbal descriptors more suitable to the average educational level of this population, and has been recently recommended by current exercise prescription guidelines as a complimentary parameter of exercise intensity.[33]

Randomization.—Participants were randomly assigned by researchers ABO and JPPM (simple randomization; 1:1:1) to receive each intervention. Participants were allocated to RLX, PA, or RLX+PA groups, following this very same order, as they agreed to participate in the interventions at the survey interviews.

Outcome Variables.—Our variables of interest were the days with headaches, duration of attacks, and pain intensity, and physical activity levels. Acute medication use was not assessed, as access to these medications is limited in this community. For the purpose of simplification, pain intensity in the diaries was categorized as 1 = "very light," 2 = "mild," 3 = "moderate," and 4 = "severe," and the short-version of the International Physical Activity Questionnaire (IPAQ) was used to assess physical activity levels.[34] IPAQ scores are expressed as metabolic equivalent of task per minute/week (METs/min/week).[34]

The primary outcome variable chosen was days with headaches. Secondary outcome variables were duration of attacks, pain intensity, and physical activity levels.

Sample Size and Statistical Analysis.—Owing to the social purpose of this study, which intended to reach a whole community, we did not establish a priori sample size calculations. Descriptive statistics are shown as mean ± standard deviation, or number/percentage of group. Differences between groups for continuous and categorical variables were computed by one-way ANOVA and chi-squared test, respectively. Between- and within-groups comparisons for clinical outcomes and physical activity variables pre and post intervention were calculated by repeated measure ANOVA with Bonferroni's corrections for pairwise comparisons. Repeated measured of one-way ANOVA with Bonferroni's corrections for pairwise comparisons was used in the analysis of the affective response to the aerobic exercise session. Eta-squared was computed as the measure of effect size. The α-value <0.05 was considered statistically significant. Statistical analyses were computed using SPSS software (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY, USA), and graphs were designed by GraphPad Prism® software (GraphPad Software Inc., Version 7.0, San Diego, CA, USA).

RESULTS

We screened 790 individuals, representing 15.3% of the total population in the riverine/rural area.

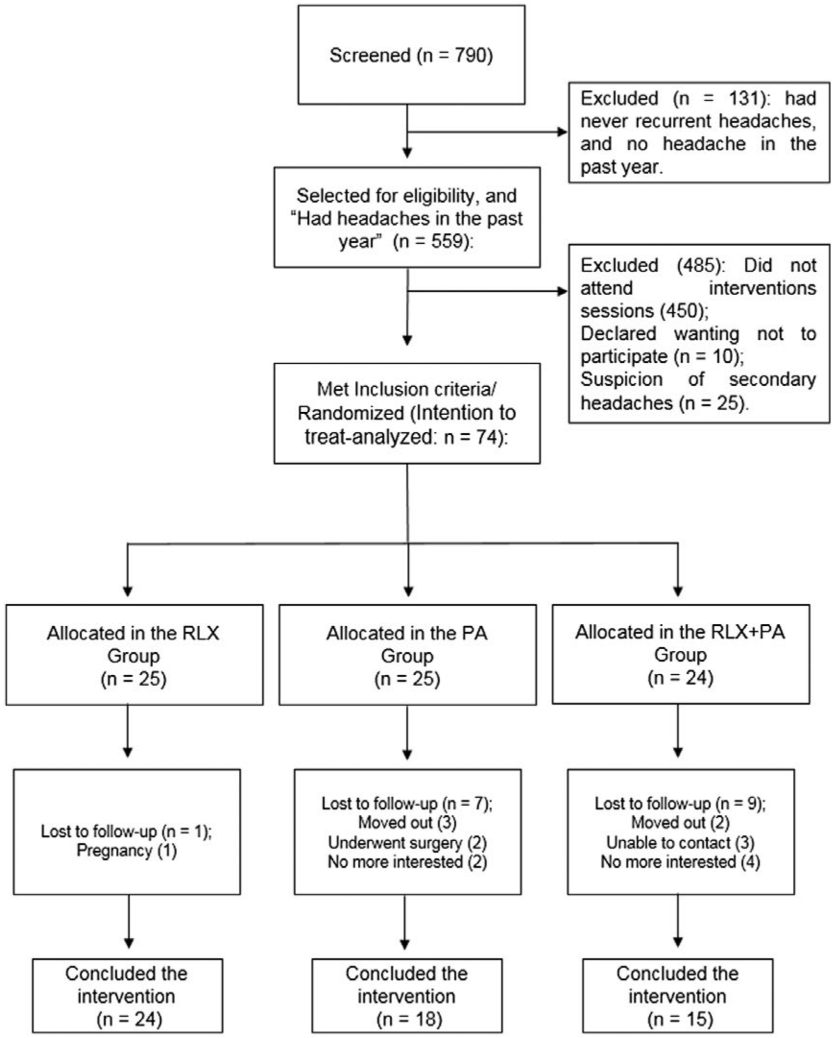

Fig. 2.—Participants' flow in the study. RLX = relaxation; PA = physical activity; RLX+PA = relaxation plus physical activity.

Figure 2 summarizes the participants' flow in the study. The 3 groups were homogeneous regarding age, sex, BMI, education, and physical activity levels (Table 1).

Attrition rates for RLX, PA, and RLX+PA groups were 14%, 28%, and 37.5%, respectively. Intention to treat analyses showed a significant main effect of time for clinical variable days with headaches [$F(1, 55) = 53.256$, $P < .001$, $\eta^2 = 0.98$], duration of attacks [$F(1, 55)$ 39.989, $P < .001$, $\eta^2 = 0.78$], and pain intensity [$F(1, 55) = 41.079$, $P < .001$, $\eta^2 = 0.8$] after 6 months of intervention (Figure 3). A posteriori power analyses of ANOVA repeated measures found β values = 0.99, 0.98, and 0.9 for the primary outcome days with headaches in the RLX, PA, and RLX+PA groups, respectively. There was a significant interaction between time and group for pain intensity [$F(2, 55) = 3.454$, $P = .039$, $\eta^2 = 0.13$]. No other significant effects were observed. Bonferroni's corrected pairwise comparisons showed that all groups had significant reductions from baseline to 6 months after intervention in days with headaches [RLX: 13.5 days (95% CI = 9.7–17.2) vs 2.5 days (95% CI = 1.3–3.6), $P < .001$; PA: 14.5 days (95% CI = 8.6–20.4) vs 3.7 days (95% CI = 1.5–5.9), $P < .001$; RLX+PA: 13.9 days (95% CI = 6.9–20.8) vs 4.2 days (95% CI = 1.3–8.7), $P < .01$, respectively] and duration of attacks [RLX: 27.8 hours (95% CI = 17.1–38.4) vs 7.6 hours (95% CI = 1.1–14.2), $P < .01$; PA: 25.7 hours (95% CI = 14–37.4) vs 2.5 hours (95% CI = 1.6–4.3), $P < .001$; RLX+PA: 25.5 hours (95% CI = 12.5–35.5) vs 4.8 hours (95% CI = 1.2–9.8), $P < .01$, respectively] (Figure 3). For pain intensity, only RLX [3.1 (95% CI = 2.7–3.5) vs 1.6 (95% CI = 1.1–2.1), $P < .001$] and RLX+PA [2.4 (95% CI = 1.9–2.9)

Table 1.—Participants' Sociodemographic and Clinical Characteristics

	Groups		
	RLX (n = 25)	PA (n = 25)	RLX+PA (n = 24)
Age (years)	41.1 ± 16.4	41.8 ± 19.7	38.0 ± 13.1
BMI (kg/m^2)	24.0 ± 7.14	27.1 ± 5.2	29.1 ± 9.2
SBP (mmHg)	118.0 ± 17.1	125.8 ± 20.4	115.7 ± 16.4
DBP (mmHg)	74.3 ± 15.9	71.8 ± 10.4	70.8 ± 12.8
Sex, n (%)			
Male	4 (16)	5 (20)	5 (20.8)
Female	21 (84)	20 (80)	19 (79.2)
Education, n (%)			
Elementary (incomplete)	20 (80)	19 (76)	19 (79.1)
Secondary	3 (12)	3 (12)	1 (4.1)
Superior	2 (8)	3 (12)	4 (16.8)
Ethnicity, n (%)			
Black	2 (8)	0 (0)	0 (0)
"Pardo"	22 (88)	21 (84)	23 (95.8)
White	3 (12)	4 (16)	1 (4.2)
Diagnose, n (%)			
EM	13 (52)	11 (44)	9 (37.5)
CM	7 (28)	6 (24)	4 (16.6)
TTH	4 (16)	7 (28)	10 (41.6)
CTTH	1 (4)	1 (4)	1 (4.2)
Time since disease onset (years)	15.8 ± 13.0	26.0 ± 17.3	20.9 ± 9.8
Days with headache (n)	13.3 ± 8.6	15.4 ± 11.0	13.3 ± 11.8
Duration of attacks (hour)	27.6 ± 23.5	28.4 ± 23.9	25.5 ± 22.5
Pain intensity (1–4)	3.0 ± 0.9	2.5 ± 0.7	2.4 ± 0.8
IPAQ (METs/min/week)	254.0 ± 551.0	448.0 ± 712.6	102.8 ± 179.9

There were no statistically significant differences between groups.
CM = chronic migraine; CTTH = chronic tension-type headache; DBP = diastolic blood pressure; EM = episodic migraine; IPAQ = international physical activity questionnaire; MET = metabolic equivalent of task; PA = physical activity; RLX = relaxation; RLX+PA = relaxation plus physical activity; SBP = systolic blood pressure; TTH = tension-type headache.

vs 1.5 (95% CI = 0.8–2.1), $P < .01$] showed significant reductions (Figure 3).

At baseline, 14% of participants met the minimum recommendations of physical activity (ie, ≥ 600 METs/min/week), while this proportion increased to 31% after the 6-month intervention period. There were a significant main effect of time [$F(1, 55) = 6.873$, $P = .011$, $\eta^2 = 0.12$] and interaction between time and group [$F(2, 55) = 4.511$, $P = .015$, $\eta^2 = 0.17$] for IPAQ. Bonferroni's corrected pairwise comparisons showed no change from baseline to 6th month in IPAQ scores in the RLX [mean difference (95% CI), −125.3 METs/min/week (−470.3, 219.6), $P = .47$] and PA [mean difference (95% CI), 327.3 METs/min/week (−71.1, 725.7), $P = .1$] groups. IPAQ scores increased in the RLX+PA group at the 6th month compared to baseline levels [mean difference (95% CI), 692.7 METs/min/week (256.3, 1129.1), $P > .01$], and compared to RLX group [mean difference (95% CI), 666.9 METs/min/week (−65, 1398.8), $P > .05$] (Figure 3).

At the physical activity sessions, wherein heart rate and the affective response were assessed, 3 participants were excluded from the analyses due to the precipitation of migraine attacks during exercise. These participants were recommended to stop the exercise session and took abortive medication. Participants' mean ± SD heart rate was 119.0 ± 23.6

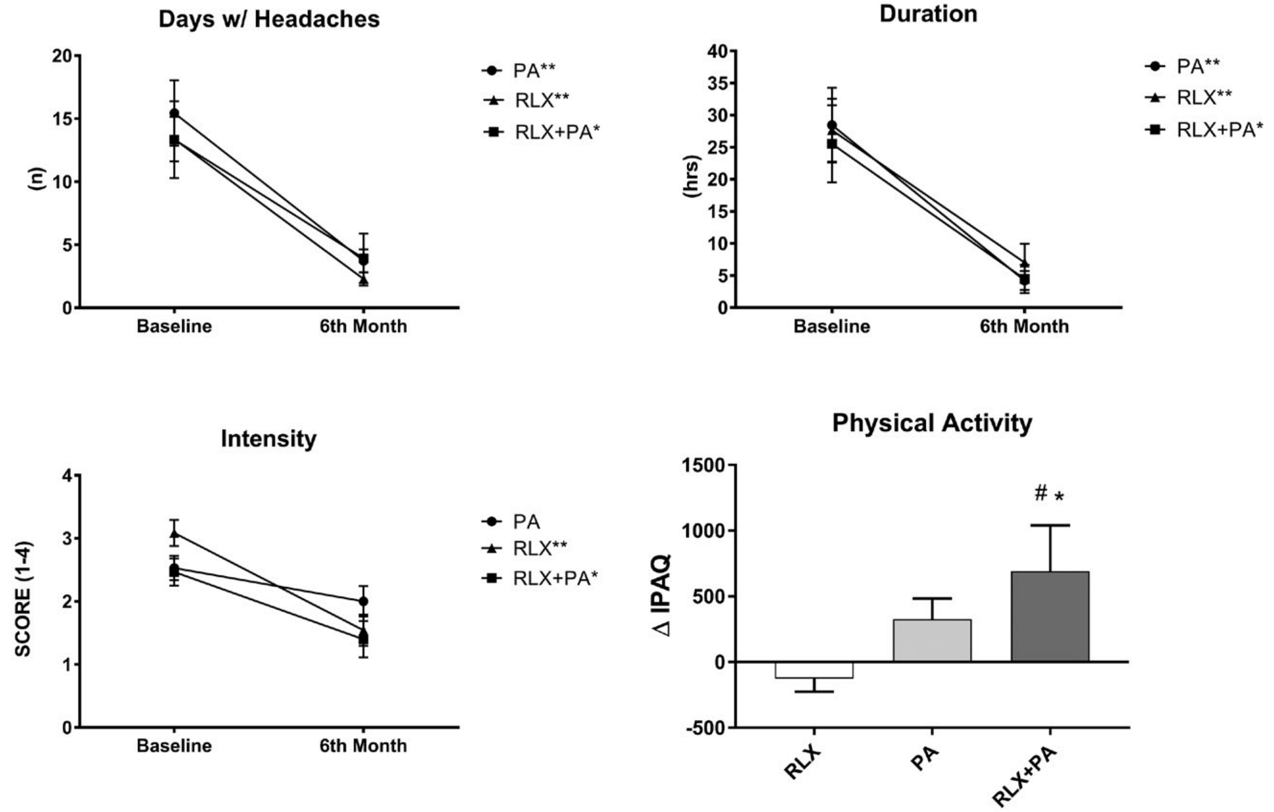

Fig. 3.—Primary (a) and secondary (b-d) outcome variables. Data are expressed as mean ± SE. RLX = relaxation; PA = physical activity; RLX+PA = relaxation plus physical activity. $^{*}P < .01$, $^{**}P < .001$, vs baseline; $^{\#}P < .05$, vs RLX. Pairwise comparisons of repeated measure ANOVA.

beats per minute, or 66% ± 10.6% of age-predicted maximal heart rate, which corresponds to the moderate exercise intensity recommended by current exercise prescription guidelines.[33,35,36]

For psychometric measures during exercise sessions, there were a main effect of time for affect scores from rest to post-exercise period [$F(1, 38) = 6.499$, $P = .015$, $\eta^2 = 0.15$] (Figure 4). Pairwise comparisons showed that post-exercise scores were significantly higher than pre-exercise values [mean (95% CI), rest = 1.6 (1, 2.1) vs post-exercise = 2.7 (2.3, 3.3), $P > .05$], meaning that, overall, participants exhibited higher well-being scores following the exercise session (Figure 4).

Per protocol analyses showed no difference in the mean monthly adherence to relaxation sessions between RLX [mean, (95% CI) = 2.7 (1.8, 3.6)] and RLX+PA [mean, (95% CI) = 2.2 (1.1, 3.4), $P = 0.9$] groups, while there was a significant inverse correlation between mean monthly adherence to the relaxation sessions and duration of headache attacks (N = 39; r = −0.31, $P < .05$). This correlation was even stronger in the RLX+PA group (N = 15; r = −0.81, $P < .01$). No other correlations were found.

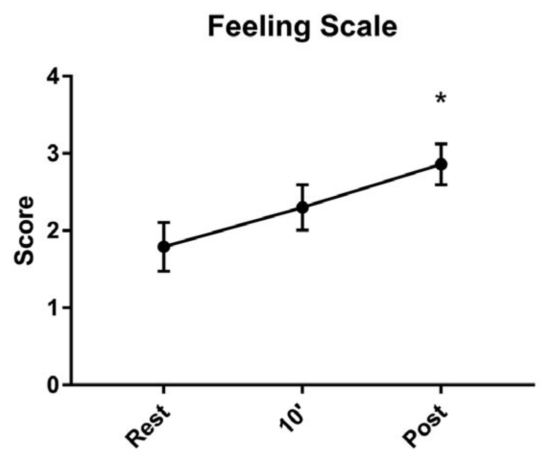

Fig. 4.—Affective response to a physical activity session (walking/jogging). Data are expressed as mean ± SE. $^{*}P < .05$, vs rest; pairwise comparisons of one-way repeated measure ANOVA.

There was no harm or adverse effect reported by the participants with any intervention.

DISCUSSION

This is a unique study because it is part of a social initiative to train and mobilize public health service workers to promote patient education and to implement interventions for primary headaches prevention in low-income communities. We found that a multidisciplinary non-pharmacological intervention through physical activity, relaxation, or the combination of both were equally effective for managing primary headaches in a low-income population. Additionally, the combination of physical activity and relaxation was also effective to change health behavior toward increased physical activity levels.

Other multidisciplinary non-pharmacological interventions in tertiary headache centers have also shown positive clinical results.[6-8] Gaul et al[7] showed that the odds ratio to achieve primary clinical outcome (≥50% reduction in headache frequency) was progressively increased as the number of lifestyle factors were addressed by the multidisciplinary staff, and it was higher in individuals within the category of 21–25 days with headaches/month. On one hand, together with our data, these studies indicate that integrating multiple health care professionals with goal-oriented approaches may be efficacious to reduce headaches and promote health behavior. On the other hand, to comply with multiple interventions may be more difficult for patients. This was confirmed in our study by a higher attrition rate observed in the combined interventions group. Likewise, even after interventions, nearly 70% of participants in our sample did not met the minimum recommendation of physical activity, and the mean monthly adherence to relaxation sessions was only 2.5 sessions.

We confirmed the preventive effect of either relaxation[7,10] or aerobic exercise[14,16] to reduce the number of headache days, or the combination of both interventions to reduce headache intensity.[13] This may reflect a synergistic effect of these interventions, which may involve common protective mechanisms. Putative mechanisms that have been ascribed for reduced headaches may include immunomodulation through the balance of pro-/antiinflammatory immune mediators (eg, cytokines),[14,16,37] modulation of the autonomic nervous system (eg, increased parasympathetic/decreased sympathetic tone),[16,38] and neuroendocrine regulation of stress response (eg, facilitation/habituation of hypothalamic-pituitary-adrenal axis).[39,40]

This study did not provide evidence for reduction on perceived stress, and whether possible reductions on this variable would be related to lower headache frequency and intensity. Nonetheless, we showed an inverse correlation between adherence to relaxation and reductions in the duration of headache attacks, with a stronger correlation in the combined interventions group. Furthermore, besides lowering perceived stress, these interventions might act on other debilitating symptoms accompanying primary headaches, such as neck pain, with positive influence on physical activity behavior as well. For example, a recent study with a cohort of patients with coexisting migraine, tension-type headache, and neck pain showed that aerobic exercise was effective to reduce headache frequency, intensity, and neck pain.[41] Interestingly, at the follow-up period, patients who reduced neck pain symptoms increased physical activity levels, suggesting reduced fear-avoidance behavior associated with musculoskeletal pain, and its negative influence on physical activity.[41] In this sense, it is tempting to speculate that relaxation and aerobic exercise may improve patients' overall function also through reduced headache-associated symptoms, such as neck pain (and fear-avoidance behavior), and thus, allow patients to engage in physical activity.

Our study also corroborated the data from physical activity behavior literature suggesting that aerobic exercise performed at a self-selected intensity elicits an elevation on positive affect, that is, increased well-being and pleasure, which can be translated into more adherence to physical activity participation.[27-31] Also, data from the heart rate-monitored sessions showed that the chosen self-selected intensity corresponded to the moderate exercise intensity preconized by current exercise prescription guidelines for health promotion.[33] Therefore, the monitoring of affective response to set the exercise intensity represent a low-cost, simple approach, and should be used to optimize long-term adherence to physical activity programs in low-income populations with no access to electronic portable devices (eg, heart rate monitors).

Of importance, in spite of the equivalent therapeutic effect observed between relaxation and physical activity, regular physical activity should be strongly encouraged for this population. There is growing evidence indicating an increased risk of cardiovascular diseases among women with migraine,[42] whereas physical activity recognizably prevents these diseases.[43] Moreover, objective measures of cardiorespiratory fitness also associated with primary headaches in a population study, with migraine being up to 4-fold more prevalent among people with low cardiorespiratory fitness.[20] Thus, implementing strategies to increase adherence to physical activity programs among primary headache patients constitutes a relevant public health issue.

Our data encourage the incorporation of non-pharmacological interventions by public health services. These constitute relatively low cost, accessible non-pharmacological interventions that can be conducted by the public health workers staff upon adequate training in low-income communities. In this regard, although the purpose of this study was not related to cost-effectiveness measures, considering public system workers' mean wage per hour of service delivered, printing costs of questionnaires, electronic devices used (ie, heart rate monitor and CD player), and the number of patients participating, a rough estimate on total costs was around US$ 2 per individual/hour of intervention.

Our study has limitations and bias that could affect its internal and external validity, such as small sample size (no a priori power calculation), performance bias (researchers and public service workers were not randomized to deliver the interventions), and study population (low socioeconomic status). Also, although it is difficult to control possible placebo effects with either relaxation or exercise interventions, the addition of a group with no intervention in the study´s design would strengthen our findings. Importantly, owing to the low educational level of this population, and the lack of expertise by the public service workers with headache data collection, one cannot rule out imprecision in the headache data retrieved. We tried to circumvent this problem by periodic contact (monthly calls) with the public workers stressing the relevant clinical information to be recorded in the diaries. Another possible source of bias was the use of prophylactic drugs. In our sample, we found that 13 (17.5%) participants were taking drugs distributed by a nationwide government health program for cardiometabolic diseases treatment, namely, angiotensin-converting enzyme (ACE) inhibitors, thiazolidinediones, and statins. ACE inhibitors constitute Level-C evidence for migraine prevention,[44] while there is recent evidence for a preventive effect of statins on episodic migraines.[45] Yet, all participants were taking these drugs for more than 6 months; therefore, it is unlikely that these medications could have influenced the clinical outcomes.

In summary, our study showed therapeutic effects with aerobic exercise and relaxation on primary headache, and the benefit on health behavior through the combination of these interventions toward increased physical activity levels. In the future, patient education and interventions programs for such populations should also address other health behaviors focusing on stress management, diet, and sleep health. A larger and more comprehensive study should also measure differences in clinical responses by headache subtypes, and the impact of such interventions on psychological/psychiatric comorbidities, such as anxiety and depression, as we perceived a large psychosocial demand in this population.

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